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Depression and violence: A Swedish total population study

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Abstract

Background: Depression increases the risk of a range of adverse outcomes including suicide, premature mortality, and self-harm, but associations with violent crime remain uncertain.

Methods: Two studies were conducted. The first study was a total population study in Sweden of patients with outpatient diagnoses of depressive disorders (n=47,158) from 2001 to 2009 was investigated. Patients were matched to general population controls (n=898,454; age and sex matched) and risk of violent crime was calculated. In addition, we compared the odds of violent crime in unaffected half-siblings (n=15,534) and full siblings (n=33,168) to the general population. In sensitivity analyses, we examined the contribution of substance abuse, socio-demographic factors, and previous criminality. In the second study we studied a general population sample of twins (n=23,020) with continuous measures of depressive symptoms for risk of violent crime.

Findings: Over a mean follow-up period of 3.2 years, 641 (3.7%) of the depressed men and 152 (0.5%) of the depressed women violently offended after diagnosis. After adjustment for socio-demographic confounders, the odds ratio of violent crime was 3.0 (95% CI: 2.8-3.3) compared to general population controls. The odds of violent crime in half-siblings and full siblings was significantly increased, showing some familial confounding of the association between depression and violence. However, the odds increase remained significant in depressed persons after adjustment for familial confounding, and in those without substance abuse comorbidity or a previous violent conviction. The mean time of follow-up in the twin study was 5.4 years, during which 88 violent crimes occurred. Depressive symptoms were associated with increased risk of violent crime and a sensitivity analysis found little difference in risk estimate when all crimes (violent and non-violent) was the outcome.

Interpretation: Risk of violent crime was increased in individuals with depression after adjustment for familial, socio-demographic and individual factors in two longitudinal studies. Clinical guidelines should consider recommending violence risk assessment in certain subgroups with depression.

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Introduction

Depression is associated with increased risk of a wide range of adverse outcomes. These include lower life-expectancy,[1] suicide,[2] self-harm,[3], acute myocardial infarction,[4] and a worse prognosis for co-occurring chronic medical conditions such as heart disease and diabetes.[5, 6] Clinical experience and expert opinion[7] also suggest an association with the risk of perpetrating violence, including homicide in male perpetrators.[8] Consistent with this, community surveys in the UK,[9] register-based investigations in Australia,[10] and cohort studies in the US,[11] and New Zealand[12] report a link with violent outcomes. However, this is not a consistent finding and no association was found in a recent US longitudinal study using lifetime[13] or past year[14] diagnoses. Moreover, in studies showing associations, they have been largely confounded by comorbid alcohol or drug use,[13] sociodemographic factors[15] or primarily found in individuals with psychotic depression.[16]

The probable reason for these inconsistencies could be that many influential studies have included large proportions of inpatients, where the actual reason for admission may have been risk of violence to others, suicidality, psychosis, or comorbid substance abuse. Since these are strong risk factors for violence,[17] they will amplify and perhaps explain any effects. Some studies have tried to control for these confounds, but none to our knowledge has also adjusted for familial effects. The latter could be a further explanation for the reported association with depression and could arise from common genetic predisposition or shared early environmental adversity. Mediating mechanisms such as impulsivity and mood instability could be important as common causes of both depression and violence.[18]

To clarify these uncertainties, we have conducted two complementary studies that benefit from using databases available for research in Sweden. In the first, we have longitudinally

followed up patients with an index diagnosis of depression to determine risks of violent crime; only outpatients were included to avoid the likely biases associated with inpatient samples. Risks of violent crime were also investigated in non-depressed siblings to determine the extent of familial confounding, and a comparison was made with risks from suicide mortality. In the second study, we have investigated the relationship between depressive symptoms and violent crime in a cohort of twins. These studies accordingly control for the major confounds we identify in the existing literature, namely socio-demographic and familial factors, as well as previous substance use disorders, self-harm, and criminal history. Because depression is common, even a small increased risk may translate into large absolute numbers. For this reason, the findings are potentially important and should inform future guidelines, since current treatment guidelines are inconsistent on assessing and managing violence risk in major depression, and lack information on risk factors.[19, 20] In contrast, self harm and suicide are, of course, already identified as being associated with depression, and guidelines[19-21] and expert opinion[22] highlight suicide risk assessment. Thus, we investigated rates of self harm and suicide mortality in the same cohort to compare risks across outcomes where clinical guidelines provide differing recommendations.

Methods

The Regional Ethics Committee at the Karolinska Institutet approved the study (2009/939-31/5). Data were merged and anonymized by an independent government agency (Statistics Sweden), and the code linking the personal identification numbers to the new case numbers was destroyed after merging, so informed consent was not required.

Study Setting

We linked several longitudinal, nationwide Swedish population registries: the National Patient , the Multi-Generation, and the National Cause-of-Death, the Swedish Twin, and the National Crime Registers. The Multi-Generation Register connects each person born in Sweden in or after 1933 and ever registered as living in Sweden after 1960 to their parents.[23] Similar information exists for those immigrants who became citizens of Sweden before age 18, together with one or both parents. Linkage of registers is possible as all residents including immigrants have a unique ten-digit personal identification number that is used in all national registers. We selected a cohort of individuals born between 1958 and 1994, which were followed from 2001 to the end of follow-up in 2009. National outpatient coverage in the Patient Register started in 2001, which was the reason that we started our follow-up at that time.

Using the Multi-Generation Register, we also identified patients with depression who had siblings, and half-siblings without depression.

Using the Swedish Twin Register, we identified young adult to middle-aged twins born between 1959 and 1986, who had participated in the Study of Twin Adults: Genes and Environment (STAGE) [24] or the Swedish Twin study of CHild and Adolescent Development (TCHAD).[25] In total, 23,020 individuals from 15,298 twin pairs (5,574 monozygotic [MZ]

and 9,724 dizygotic [DZ] pairs) are included in the current study. Zygosity was determined using DNA testing or validated zygosity questionnaires.

Individuals with depression

Cases with depression were identified from the National Patient Register as having at least two outpatient episodes between 2001 and 2009 according to ICD-10 (codes F32-F33.9).[26] We excluded those with inpatient episodes of depression to avoid reverse causality (as violence and aggression may precipitate admission), and those with inpatient or outpatient diagnoses of schizophrenia, schizophrenia-spectrum, and bipolar disorder between 1969 and 2009.

In the twin study, depressive symptoms were measured by a short form of the Center for Epidemiologic Studies Depression (sCESD) Scale.[27] The sCESD scale included 11 items, and each item was rated on a 4-point scale (0 = not at all or almost not at all; 1 = rather rarely; 2 = quite often; 3 = all the time or almost all the time). A sum score was created based on the 11 items, with good reliability (Cronbach's alpha = 0.86). Most of the twins answered the questionnaires in 2005, and they were followed for any outcome through linkage to the crime register.

Diagnostic validity

Swedish patient register data on diagnoses have good to excellent validity for a range of conditions, including bipolar disorder[28] and schizophrenia.[29] Overall, the positive predictive value of the inpatient register, in a recent review, was found to be 85%–95% for most diagnoses.[30] For the purposes of this study, we examined the validity of diagnoses of depression in a separate sample of patients with depression, by comparing concordance rates between patient register diagnoses (as we have used) and another clinical register that

provided standardized consensus diagnoses involving comprehensive court-ordered multidisciplinary evaluations over 4 weeks in inpatient settings,[31] the latter which acted as a gold standard. In this sample of 3,059 patients assessed between 1996 and 2001, we found fair to moderate agreement (κ of 0.32; 88% full agreement).

The mean sCESD depression score of twins who had a lifetime diagnosis of depression from the National Patient Register (mean score 13.1, 95% CI: 12.7-13.6) was substantially higher than twins without a diagnosis of depression (mean 7.0, 95% CI: 6.9-7.1).

Only around 1% of hospital admissions have missing personal identification numbers.[32]

Outcome Measures

Data on convictions for violent crime during the years 1972–2009 were retrieved for all individuals in the cohort from the National Crime Register, which includes conviction data on all persons aged 15 years (the age of criminal responsibility) and older. These data were extracted both before (as covariate) and after diagnosis (as outcome) of depression. Conviction of a violent offence was defined as homicide and attempted homicide, aggravated assault (an assault that is life-threatening or leads to severe bodily harm), common assault, robbery, arson, any sexual offense (rape, sexual coercion, child molestation, and sexual harassment [including indecent exposure]), and illegal threats or intimidation.[32] Conviction data were used because the Criminal Code in Sweden determines that individuals are convicted as guilty regardless of mental illness (i.e., being judged as not guilty by reason of insanity is not a possibility). Thus, conviction data included persons who received custodial or noncustodial sentences and people transferred to forensic psychiatric hospital. Furthermore, conviction data included individuals cautioned or fined (which are more likely to be used in juvenile cases). In addition, though certain factors may affect sentencing, plea-

bargaining at the conviction stage is not part of the Swedish legal system.[33] Therefore, conviction data more accurately reflect the extent of officially resolved criminality in the population. The crime register has total national coverage—only 0.05% of all registered convictions had incomplete personal identification numbers during the years 1988–2000.[32]

Data on cause of death were retrieved for all individuals who died between 1969 and 2009. The Cause of Death register is based on death certificates and covers over 99% of all deaths.[34] Suicides included undetermined deaths (ICD codes Y10-Y34) as their exclusion would underestimate actual rates.[35] Data on self-harm were retrieved from the National Patient Register, and included certain (ICD codes X60-X84) and uncertain self-harm (ICD codes Y10-Y34).

Socio-demographic and psychiatric covariates

Family disposable income at age 15 (divided into thirds) was used as a proxy for income, and used as a dichotomous variable (lowest tertile vs. top two tertiles). If this was unavailable, family disposable income, at age 16 was used or until the age when it became available. Single marital status was defined as being unmarried at first diagnosis. Immigrant status was defined as being born outside of Sweden. Imputation or other methods were not used to replace missing family income data (0.7%).

Drug and alcohol use disorders were defined using inpatient (1969–2009) and outpatient (2001–2009) primary or secondary diagnoses of alcohol or drug abuse or dependence (ICD-8: 303, 304; ICD-9: 303, 304, 305.1, 305.9; ICD-10: F10-F19, except x.5.). The diagnostic validity of this secondary diagnosis is moderate.[36]

Analyses

For each patient, up to twenty general population control individuals without any diagnosis of depression were matched individually by birth year and sex. We estimated the association with having been diagnosed with depression, as per related work using matched controls,[36, 37] using the clogit command in Stata, version 12.1 (StataCorp). The clogit command fits conditional (fixed effects) logistic regression models to matched case–control groups. We included two confounders (low family income, and immigrant status) on theoretical grounds, based on related work in severe mental illness,[36, 38] and also tested whether they were each independently associated with either case or control and outcome measures, respectively, in univariate analyses at the 5% level of significance.[39] We also conducted stratified subanalyses by sex, previous criminality, self-harm history, and drug and alcohol abuse.

Sibling control studies

To account for possible familial confounding, we conducted additional analyses using unaffected full siblings and half-siblings of patients as controls. In these analyses, we identified full siblings (n=33,519), maternal half-siblings (n=8,734), and paternal half-siblings (n=6,800), and these individuals were each compared with 20 age and sex-matched general population controls using matched conditional logistic regression. Analyses were adjusted for low family income and immigrant status, and odds ratios of violence were reported.

We then compared patient analyses to sibling analyses using ratios of odds ratios (ROR).[40] The ROR takes into account the increased risk of violence in unaffected siblings (Figure 1). An ROR of 1.0 would mean that the risk of violence in those with depression (compared to the general population) is the same as the risk in their unaffected siblings (compared to the general population), i.e. the association between depression and violence is fully confounded by environmental and genetic factors shared by siblings.

Sensitivity analyses

We conducted four sensitivity analyses on the main sample. First, we examined those with at least one inpatient diagnosis 2001-2009 (i.e. patients who are excluded from the main analyses), and compared risk of violent crime with age and gender matched population controls. Adjustments were made for income and immigrant status.

Second, we excluded patients with depression with comorbid personality disorder. Comorbid personality disorder is common in patients with depression[41] and is associated with violence,[42] and hence excluding it would further test our primary hypothesis. Third, we restricted violent crime to specific outcomes where interpersonal violence is known to have occurred - homicide and attempted homicide, and all forms of assault (including aggravated, and assault of an officer). This meant that we excluded arson, sexual offences, and threats and intimidation. Separately, we also examined rates and odds of violent crime, by type of crime. Finally, we examined odds of violent crime specifically within 3, 6, and 12 months of the first diagnosis of depression to exclude patients who may have recovered from depression at the time of the outcome.

In relation to the sibling analyses, we excluded (1) older siblings and (2) younger siblings to avoid violence or depression in one group affecting the other, and (3) excluded those siblings with follow-up beginning before 2001 when outpatient data was unavailable.

Co-twin control study

We conducted co-twin control analyses to evaluate whether the observed association between depression and violent crime was due to common genetic or environmental influences.[43] The twins were followed from the time of answering the questionnaire until any violent crime or end of study.[43] First, standard Cox regression models were applied to estimate the association

between sCESD score and violent crime, adjusting for age (at the time of answering the questionnaire) and sex, with robust standard error accounting for twin clustering. Second, stratified Cox regression models were applied to estimate the association between sCESD score and violent crime in MZ and DZ twin pairs separately.

STROBE guidelines were followed.

Results

Population and sibling sample

We identified 47,158 individuals (17,249 men, and 29,909 women) with outpatient diagnoses of depression between 2001 and 2009 (descriptive statistics in Table 1). Men had a mean age at first diagnosis of 31.5 (SD=10) and women 30.7 (SD=10.0). The mean time of follow-up was 3.0 years for men and 3.2 years for women.

During follow-up, 641 men (3.7%) and 152 (0.5%) women with depression committed a violent crime, compared to 1.2% of men and 0.2% of women in age and sex matched controls.

Those with depression were thus at a 3-fold increased odds of violent crime when compared to general population controls (adjusted OR[aOR]=3.0, 95% CI: 2.8-3.3). The odds of violent crime were between 1.1 and 1.7 for both full and half-siblings, compared to general population controls. There was a trend for higher figures in the full siblings, as would be predicted by a genetic model. By comparing odds ratios in cases and sibling analyses, indirect comparisons can be made of cases compared with siblings (Figure 1). These analyses demonstrated that depressed persons had a two-fold increased odds of violent crime risk compared with their unaffected siblings (Table 2).

The odds of violent crime were similar for men with depression (compared to men without depression) and women with depression (compared to women without depression), and the ***relative*** risk increase remained significant when we excluded a history of previous violent and non-violent crimes, self-harm, and substance use disorders in both cases and controls (Table 2). However, the presence of these pre-existing background factors led to notable changes in ***absolute*** risks of violent crime. A previous offending history had the largest effect - 12.5% of men with this history committed a violent crime after depression diagnosis; 3.8%

in women did so. The rates were further increased by addition of substance misuse and/or self-harm (Table 3). Combinations of risk factors increased absolute risk of violent crime to above 15% in men, although the number of individuals with these combinations of risk factors was low (Table 3).

Sensitivity analyses

In those with inpatient diagnoses over 2001-2009, the adjusted odds ratio of violent crime was higher at 5.7 (95% CI: 5.2-6.2). In patients with depression, 3,813 (8%) had a comorbid personality disorder: excluding those had no demonstrable impact on the aOR of violence (aOR=3.1, 95% CI: 2.8-3.3; compared to an aOR=3.0, 95% CI: 2.8-3.3 in the whole sample). No significant differences were found when restricting outcomes to specific interpersonal crimes (homicide and attempted homicide, and all forms of assault) (aOR=2.9, 95% CI: 2.6-3.1). Rates and odds by type of violent crime are reported in the appendix (p 1). Non-significantly higher odds ratios were found when specifically examining violent crime within 3 months (aOR=3.6, 95% CI: 2.8-4.5; 87 violent crimes in depression sample), 6 months (aOR=3.3, 95% CI: 2.8-4.0; 135 violent crimes), and 12 months (aOR=3.6, 95% CI: 3.2-4.1; 346 violent crimes) of first diagnosis compared to 3.2 years of follow-up (793 violent crimes).

In sensitivity analyses of the sibling sample (appendix pp 2-4), we found no significant differences when 1) including only older siblings, 2) including only younger siblings, 3) excluding siblings with follow-up before 2001.

Self-harm and suicide mortality

Over a mean follow-up of 3.2 years, 575 (3.3%) men and 1,287 (4.3%) women self-harmed (appendix p 5). These rates are comparable to the rates of violent crime described above for

men, but higher for women. Self-harm in individuals with depression was increased compared to the general population (aOR=5.7, 95% CI: 5.4-6.0). In the same period, 100 (0.6%) men and 41 (0.1%) women died from suicide (appendix p 5). Death by suicide was increased in patients compared to the general population (aOR=6.7, 95% CI: 5.5-8.1), and full siblings (ROR=2.9, 95% CI: 2.2-3.8).

Twin sample

In the twin sample (9,834 men and 13,186 women), the mean age at questionnaire completion was 32.7 (SD=8.2) for men and 32.5 (SD=8.2) for women. The mean sCESD score was 6.9 (SD=5.1) for men and 7.6 (SD=5.9) for women. The mean time of follow-up was 5.3 years for men and 5.4 years for women. During follow-up, 73 men (0.7%) and 15 (0.1%) women committed a violent crime, with a mean time-to-event of 1.5 years for men and 1.6 years for women.

There was a significantly increased risk of violent crime in those with more depressive symptoms (Table 4). Statistical power was limited for further analyses of the twins by zygosity. In a sensitivity analysis of the twin sample, any crime was also significantly associated with increased depressive symptoms (HR=1.07, 1.01-1.09).

Discussion

In this population-based study, we investigated absolute and relative risks of violent crime after diagnosis of depression. In 47,158 individuals with depression, we found a three-fold increased odds of violent crime after adjustment for socio-demographic factors - this rate remained significantly elevated when we excluded patients with a previous history of substance abuse, any criminality, or self-harm. The association remained significant after adjustment for familial confounding, although the strength of the association was reduced. In other words, even after adjusting for genetic and early environmental factors, a depression diagnosis modestly increased the risk of violent crime.

Comparing maternal and paternal half-siblings provides some indication whether the familial association is explained primarily by early environmental factors or whether it is by genes. If the risk attenuation had been stronger in the maternal half-siblings, this would suggest early environmental confounding as it is assumed that half-siblings share more environment if they share a mother rather than a father. In fact, the odds of violence were similar in maternal and paternal half-siblings, suggesting that the confounding is mostly genetic. The mediating mechanism translating genetic risk is not known. One possibility is that comorbid personality disorders could partly explain the relationship. However, excluding those with register-based diagnoses of personality disorder did not affect our results. Nevertheless, registry diagnoses only capture a selection of individuals with personality problems and more sensitive markers of personality and disease may be more informative. Impulse control and affect regulation may be among the underlying mechanisms,[18] which may also explain increased violence risk in other psychiatric disorders.

An important potential implication of our findings relates to interpretion of safety data on antidepressants. Anecdotally, antidepressants have been associated with self-harm and severe

violence, which drew considerable attention in the public and media a decade ago.[44] The reduction of antidepressant prescribing to young people that followed failed to reduce rates of self-harm, with recent evidence suggesting that, in the US, self-harm rates actually increased.[45] Although our study does not bear directly on the association between antidepressants and violence, it suggests that a diagnosis of depression will confound interpretation of the effects of treatment for depression on violence (and self harm). Therefore pharmacovigilance data on antidepressants needs to be interpreted with considerable caution.

Panel: **Research in context**

Systematic review

We searched Medline from 1946 up to November 6, 2014, with no language or date restrictions, for articles on depression and violence using genetically informed designs. The following search terms were used: ("depress*" or "unipolar*" or "affect*") and ("sibling*" or "twin*") and ("viol*" or "homicide" or "crim*"). We identified no studies. Further, we searched Medline specifically for systematic reviews (using the same search terms but without 'sibling' or 'twin') and again identified no reviews.

Interpretation

We have reported the first family based studies of violence risk in depression. Our findings suggest that the odds of violent crime are two to three fold after adjustment for familial, socio-economic and individual factors. Absolute rates of violent crime were low in the overall population-based investigation in men (3.7%) and markedly lower in women with depression (0.5%), although certain subgroups with histories of substance misuse and/or violent crime were associated with rates of more than 15% in men.

Strengths and Limitations

Our study benefits from several strengths. First, the use of population registers allowed us to obtain a large sample size. Furthermore, through register linkage we were able to exclude the more extreme cases of depression, those with inpatient episodes. In a sensitivity analysis, we found odds of violent crime that were around double in those with inpatient histories compared to outpatient groups, underscoring our decision to exclude these patients. In terms of generalizability, other work has found that over 2006-2008, 3.6% of depressed patients were hospitalized.[46] By using genetically informed designs (half-siblings and siblings), we

were able to examine the possibility of genetic and early environmental confounding behind the reported association between depression and violence. Different methods to assess depression were used - clinical diagnoses in the population study and a continuous symptom measure in the twin investigation. In addition, sensitivity analyses found similar patterns for diagnoses of depression that were made within 3, 6, and 12 of violent crime, and separately for a related outcome, namely all crimes.

Limitations of our study include limited statistical power for our twin study to test for genetic confounding. As we relied on patient registers, we did not have information on depressed persons who present to primary care alone, and will not enter patient registers. Other Swedish research has demonstrated that 47% of community persons with DSM-IV diagnoses of depression seek medical care. In those that seek medical services, 26% receive GP care alone but these individuals have milder symptoms than those accessing psychiatric services.[47] At the same time, there is an advantage in focusing on those who present to secondary care as longer assessments and interventions can be offered than in primary care. To partly address this limitation, we additionally used twin data as this was a general (non-patient) sample. Another limitation is that we did not account for the effects of treatment as these data are only available from mid-2005, require different designs to examine,[48] and will be investigated separately. A final limitation is that this study was done in one country, which could affect generalizability. However, the prevalence of violent assault in Sweden is similar to that in other high-income countries,[49] and a Swedish study estimated the point prevalence of major depression at 5.2%,[50] compared to 6.7% in the US,[51] and 6.3% in Australia.[52]

Risk assessment and violence

It is standard clinical practice that risk assessment in depression considers suicidal outcomes. Do the absolute risks of violence in depression presented here warrant changes to clinical

guidelines, which currently make inconsistent recommendations regarding violent outcomes?[19-21] The absolute risk of violent offending after diagnosis was 3.7% in the men with depression and 0.5% in women. US clinical depression guidelines state that violence and suicide risk should be monitored, and indicate that history of violence is a risk factor.[19] In contrast, National Institute for Health and Care Excellence (NICE) guidelines do not discuss violence risk.[20] The absolute rates of violence we have reported are certainly lower than similarly designed studies in other mental illnesses. However, we found in certain depressive subgroups (see Table 3), such as those with histories of both violent crime and substance abuse or self-harm, rates of violent crime of over 15% during the approximately 3 year follow-up. By comparison, absolute rates in men are higher in schizophrenia at around 10% for similar time at risk[53] and 8% with bipolar disorder.[54] Guidelines are also inconsistent for these disorders as well. In schizophrenia, all newly diagnosed patients should be risk assessed according to NICE and US guidelines.[55, 56] In bipolar disorder, this is not the recommendation.[57]

In contrast, clinical guidelines are consistent about the need for suicide risk assessment in depression, schizophrenia, and bipolar disorder. The recent WHO publication on suicide prevention, for example, recommends detailed evaluations of suicide risk in depression.[22] However, in the present study, rates of self-harm for men were actually lower than rates of violent crime, and, of course, suicide mortality considerably lower (appendix p 5). In terms of population impact, the association of violence with depression will be more important than with other diagnoses because depression is a considerably more prevalent condition. Risk assessment remains prone to high false positive rates,[58] but the consequences of classifying patients with depression into higher risk groups (by gender and pre-existing risk factor) should mitigate against potential harms. Indeed, those identified as high risk could potentially benefit from psychological interventions as has been demonstrated for suicidality in

depression.[59] Trials investigating whether drug or psychosocial interventions reduce violence could be of great interest in high risk samples.

In conclusion, the association between a depression diagnosis and violent crime has been demonstrated, independent of potential confounders and using two complementary designs. The magnitude of the effects, certainly when compared with those for self harm in the same population, suggest that the assessment of the risk of violence should be considered routinely for some individuals with clinical depression and potentially included more consistently in clinical guidelines.

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Figure 1. Ratio of Odds Ratio

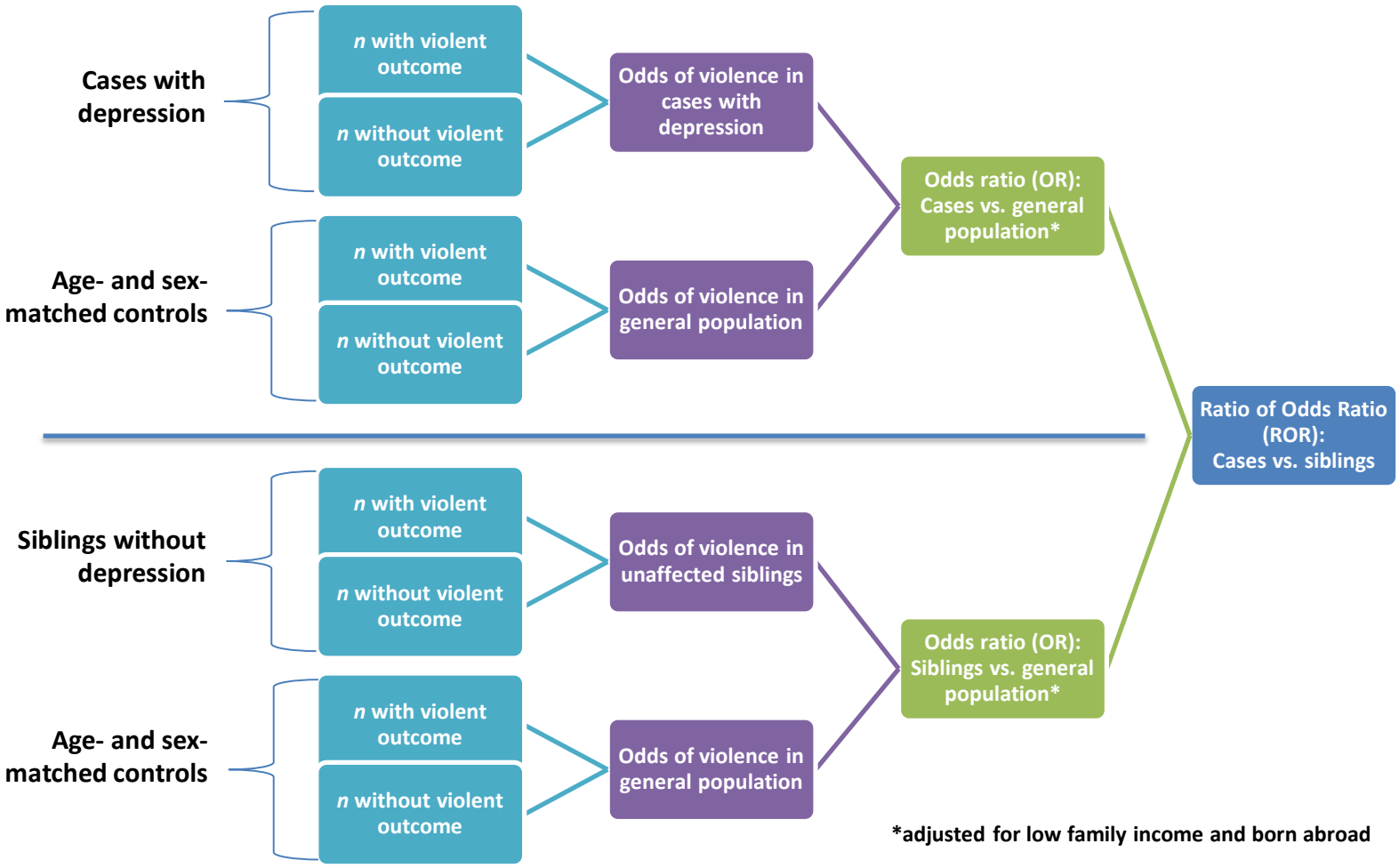

Table 1: Descriptive data on risk factors for individuals with outpatient diagnoses of depression

	Depression		Siblings		Maternal half-siblings		Paternal half-siblings		General population	
	Men (n=17,249)	**Women (n=29,909)**	**Men (n=14,211)**	**Women (n=18,957)**	**Men (n=3,519)**	**Women (n=3,281)**	**Men (n=4,517)**	**Women (n=4,217)**	**Men (n=329,307)**	**Women (n=569,147)**
SE factors										
Age at 1st diag (SD)	31.5 (10.0)	30.7 (10.0)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Income in lowest tertile	4,835 (28.2%)	8,093 (27.3%)	2,298 (16.2%)	3,422 (18.1%)	873 (25.0%)	895 (27.5%)	1,267 (28.5%)	1,229 (29.7%)	81,122 (24.6%)	143,941 (25.3%)
Born abroad	3,520 (20.4%)	5,417 (18.1%)	927 (6.5%)	1,324 (6.9%)	47 (1.3%)	47 (1.4%)	138 (3.1%)	119 (2.8%)	60,530 (17.6%)	105,114 (17.7%)
Single	11,582 (67.1%)	17,862 (59.7%)	---	---	---	---	---	---	205,549 (59.8%)	321,175 (54.0%)
Individual factors before diagnosis										
Alcohol abuse	902 (5.2%)	836 (2.8%)	294 (2.0%)	198 (1.0%)	100 (2.8%)	48 (1.5%)	102 (2.3%)	55 (1.3%)	4,818 (1.4%)	5,563 (0.9%)
Drug abuse	715 (4.1%)	620 (2.1%)	173 (1.2%)	135 (0.7%)	72 (2.0%)	36 (1.1%)	74 (1.6%)	44 (1.0%)	2,811 (0.8%)	2,964 (0.5%)
Alcohol crime	565 (3.3%)	99 (0.3%)	195 (1.4%)	32 (0.2%)	96 (2.7%)	17 (0.5%)	109 (2.4%)	10 (0.2%)	2,791 (0.8%)	629 (0.1%)
Drug crime	770 (4.5%)	209 (0.7%)	235 (1.6%)	73 (0.4%)	97 (2.8%)	23 (0.7%)	109 (2.4%)	25 (0.6%)	3,506 (1.0%)	1,457 (0.2%)
Alc/drug medication	253 (1.5%)	108 (0.4%)	39 (0.3%)	12 (0.1%)	6 (0.2%)	0 (0.0%)	5 (0.1%)	3 (0.1%)	713 (0.2%)	455 (0.1%)
Any crime	6,213 (36.0%)	3,549 (11.9%)	3,485 (24.3%)	1,330 (6.9%)	1,226 (34.8%)	336 (10.2%)	1,514 (33.5%)	401 (9.5%)	67,942 (19.8%)	33,352 (5.6%)
Violent crime	2,322 (13.5%)	572 (1.9%)	1,080 (7.5%)	188 (1.0%)	408 (11.6%)	56 (1.7%)	501 (11.1%)	54 (1.3%)	19,068 (5.5%)	4,071 (0.7%)
Non-violent crime	5,749 (33.3%)	3,282 (11.0%)	3,268 (22.8%)	1,262 (6.6%)	1,152 (32.7%)	310 (9.4%)	1,420 (31.4%)	384 (9.1%)	62,756 (18.3%)	31,485 (5.3%)
Self-harm	910 (5.3%)	2,362 (7.9%)	278 (1.9%)	509 (2.7%)	94 (2.7%)	146 (4.5%)	101 (2.2%)	135 (3.2%)	5,187 (1.5%)	11,114 (1.9%)

Income data was missing for 121 men and 253 women with depression, 134 men and 214 women full siblings, 32 men and 23 women maternal half-siblings, 72 men and 85 women paternal half-siblings, and 14,341 men and 25,712 women general population controls.

Table 2: Adjusted odds ratios (aORs) of violent crime in patients with depression, in unaffected siblings, and general population controls

	General population n=47,158	Paternal half-sibling n=6,800		Maternal half-sibling n=8,734		Full sibling n=33,516	
	aOR	aOR	ROR	aOR	ROR	aOR	ROR
Overall	3.0 (2.8-3.3)	1.2 (1.1-1.4)	2.5 (2.2-2.9)	1.2 (1.1-1.4)	2.5 (2.2-2.8)	1.5 (1.3-1.6)	2.1 (1.8-2.4)
Gender							
Male	3.1 (2.9-3.4)	1.2 (1.1-1.4)	2.5 (2.2-2.9)	1.2 (1.1-1.4)	2.5 (2.2-3.0)	1.4 (1.3-1.6)	2.2 (1.9-2.5)
Female	2.8 (2.3-3.3)	1.2 (0.9-1.5)	2.4 (1.7-3.3)	1.2 (0.9-1.6)	2.3 (1.6-3.2)	1.7 (1.4-2.2)	1.6 (1.2-2.1)
Without previous:							
Alc/drug	3.0 (2.8-3.3)	1.2 (1.1-1.4)	2.5 (2.2-2.9)	1.2 (1.0-1.3)	2.6 (2.2-3.0)	1.4 (1.3-1.6)	2.1 (1.9-2.4)
Violent crime	3.0 (2.7-3.3)	1.2 (1.0-1.3)	2.6 (2.2-3.0)	1.2 (1.1-1.4)	2.4 (2.0-2.9)	1.5 (1.3-1.6)	2.1 (1.8-2.4)
Any crime	2.7 (2.4-3.1)	1.1 (0.9-1.3)	2.4 (1.9-3.0)	1.3 (1.1-1.6)	2.0 (1.6-2.5)	1.4 (1.2-1.6)	1.9 (1.5-2.3)
Self-harm	3.1 (2.8-3.4)	1.2 (1.1-1.3)	2.6 (2.2-3.0)	1.2 (1.1-1.4)	2.5 (2.2-2.9)	1.4 (1.3-1.6)	2.1 (1.9-2.4)
All of above	2.6 (2.3-3.0)	1.1 (0.9-1.3)	2.3 (1.9-2.9)	1.3 (1.1-1.6)	2.0 (1.6-2.5)	1.4 (1.2-1.6)	1.9 (1.5-2.3)

General population controls are matched by age and sex. aOR analyses are adjusted for low family income and being born abroad. ROR is Ratio of Odds Ratios.

Table 3. Prevalence of risk factors and rates of violent crime in individuals with depression with different background risk factors.

Risk factor before diagnosis	Prevalence of risk factor by subgroup		Prevalence of violence by subgroup	
	Men (n=17,249) % (n)	Women (n=29,909) % (n)	Men % (n)	Women % (n)
Overall	n/a	n/a	3.7% (641)	0.5% (152)
(1) Substance abuse	8.5% (1,466)	4.5% (1,353)	8.9% (131)	2.1% (28)
(2) Self-harm	5.3% (910)	7.9% (2,362)	6.5% (59)	1.4% (34)
(3) Violent crime	13.5% (2,322)	1.9% (572)	12.5% (291)	3.8% (22)
(1) and (2)	1.6% (279)	1.4% (423)	9.3% (26)	2.1% (9)
(1) and (3)	3.0% (524)	0.4% (115)	16.2% (85)	5.2% (6)
(2) and (3)	1.5% (266)	0.4% (127)	15.0% (40)	7.9% (10)
(1), (2), and (3)	0.7% (123)	0.1% (42)	16.3% (20)	9.5% (4)
Not (1), (2), or (3)	78.2% (13,497)	87.7% (26,245)	2.2% (291)	0.3% (89)

Table 4. Association between depression and violent crime: co-twin control analyses (Hazard ratios with 95% confidence intervals).

Exposure	Outcome	Standard Cox regression in all twins n=23,020		Stratified Cox regression in MZ twins n=8,903		Stratified Cox regression in DZ twins n=14,117	
		n	HR (95% CI)	n	HR (95% CI)	n	HR (95% CI)
1- sCESD	Violent crime	88	1.09 (1.06-1.13)	32	0.98 (0.82-1.18)	56	1.07 (0.91-1.26)

Hazard ratios reflected the in changes in hazards of outcome with one unit change in the short form of the Center for Epidemiologic Studies Depression (sCESD) Scale. MZ, monozygotic; DZ, dizygotic.